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CLAIMS

What is Claimed Is:

- 10 1.) An isolated nucleic acid derived from a human gene encoding a protein selected from a member of the group consisting of aminopeptidase P protein (XPNPEP2), bradykinin receptor B1 protein (BDKRB1), tachykinin receptor 1 protein (TACR1), C1 esterase inhibitor protein (C1NH), kallikrein 1 protein (KLK1), bradykinin receptor B2 protein (BDKRB2), angiotension converting enzyme 2 protein (ACE2), and
- 15 protease inhibitor 4 protein (PI4), wherein said nucleic acid comprises at least one polymorphic position.
- 2.) The isolated nucleic acid of claim 1 wherein said at least one polymorphic position for each said gene is a polymorphic position specified in Table V, or complement thereof.
- 20 3.) The isolated nucleic acid of claim 2 wherein the sequence at said at least one polymorphic position is depicted in a nucleic acid sequence selected from the group consisting of SEQ ID NO: 163 to 288; 643 to 706; and 910 to 961, and 1574 to 1575, or complement thereof.
- 25 4.) The isolated nucleic acid of claim 3 wherein said at least one polymorphic position resides in a non-coding position within the genomic sequence of said gene.
- 5.) The isolated nucleic acid of claim 3 wherein said at least one polymorphic position resides in a coding position within the genomic sequence of said gene.
- 30 6.) The isolated nucleic acid of claim 5 wherein said at least one polymorphic position residing in a coding position results in a missense mutation of the translated product of said gene.
- 35 7.) The isolated nucleic acid of claim 5 wherein said at least one polymorphic position residing in a coding position results in a silent mutation of the translated product of said gene.

- 5 8.) The isolated nucleic acid of claim 4 wherein said at least one polymorphic position residing in a non-coding position resides within the untranslated region of said gene.
- 9.) The isolated nucleic acid of claim 4 wherein said at least one polymorphic position residing in a non-coding position resides within
- 10 an intronic region of said gene.
- 10.) The isolated nucleic acid of claim 8 wherein said at least one polymorphic position is selected from the group consisting of:
- a.) 62738 of the human bradykinin receptor B2 genomic sequence;
- 15 b.) 4627 of the human kallikrein 1 genomic sequence; and
- c.) 74651 of the human aminopeptidase P genomic sequence.
- 11.) The isolated nucleic acid of claim 10 wherein said at least one polymorphic position is selected from the group consisting of:
- a.) 62738T of the human bradykinin receptor B2 genomic
- 20 sequence;
- b.) 62738A of the human bradykinin receptor B2 genomic sequence;
- c.) 4627C of the human kallikrein 1 genomic sequence;
- d.) 4627T of the human kallikrein 1 genomic sequence;
- 25 e.) 74651C of the human aminopeptidase P genomic sequence; and
- f.) 74651T of the human aminopeptidase P genomic sequence.
- 12.) The isolated nucleic acid molecule according to claim 11, wherein said nucleic acid sequence is at least 30 nucleotides in length.
- 30 13.) The isolated nucleic acid molecule according to claim 11, wherein said nucleic acid sequence is at least 40 nucleotides in length.
- 14.) A probe that hybridizes to a polymorphic position defined in claim 2.
- 15.) The probe of claim 14 wherein said probe is at least 15 nucleotides in length.
- 35 16.) The probe of claim 15 wherein a central position of the probe aligns with said polymorphic position.

- 5 17.) The probe of claim 15 wherein the 3' end of the primer aligns with said polymorphic position.
- 10 18.) A method of analyzing at least one nucleic acid sample, comprising the steps of (1) obtaining said nucleic acid sample from one or more individuals; and (2) determining the nucleic acid sequence at one or more polymorphic positions in a gene encoding a protein selected from the group consisting of aminopeptidase P protein (XPNPEP2), bradykinin receptor B1 protein (BDKRB1), tachykinin receptor 1 protein (TACR1), C1 esterase inhibitor protein (C1NH), kallikrein 1 protein (KLK1), bradykinin receptor B2 protein (BDKRB2), angiotension converting enzyme 2 protein (ACE2), and protease inhibitor 4 protein (PI4).
- 15 19.) The method according to claim 18, further comprising the steps of (3) testing each individual for the presence of a disease phenotype; and (4) correlating the presence of the disease phenotype with the sequence at said one or more polymorphic positions.
- 20 20.) The method according to claim 19, wherein said one or more polymorphic position of said nucleic acid sequence is a polymorphic position specified in Table V for said gene.
- 25 21.) The method according to claim 20, wherein the nucleic acid sequence at said one or more polymorphic position is depicted in a nucleic acid sequence selected from the group consisting of SEQ ID NO:163 to 288; 643 to 706; and 910 to 961, and 1574 to 1575, or complement thereof.
- 30 22.) A method of constructing haplotypes using the isolated nucleic acids of claim 1, comprising the step of grouping at least two said nucleic acids.
- 23.) The method according to claim 22 further comprising the step of using said haplotypes to identify an individual for the presence of a disease phenotype, and correlating the presence of the disease phenotype with said haplotype.
- 35 24.) The method according to claim 19 further comprising the step of quantifying the nucleic acid sample comprising the polymorphic base.

- 5 25) The method according to claim 21 or 23 wherein the disease phenotype is angioedema or an angioedema-like disorder.
- 26) The method according to claim 25 wherein the polymorphic position is a member of the group consisting of:
- a.) 62738 of the human bradykinin receptor B2 genomic sequence;
- 10 b.) 4627 of the human kallikrein 1 genomic sequence; and
- c.) 74651 of the human aminopeptidase P genomic sequence.
- 27) The isolated nucleic acid of claim 26 wherein the sequence at the polymorphic position is a member of the group consisting of:
- 15 a.) 62738T of the human bradykinin receptor B2 genomic sequence;
- b.) 62738A of the human bradykinin receptor B2 genomic sequence;
- 20 c.) 4627C of the human kallikrein 1 genomic sequence;
- d.) 4627T of the human kallikrein 1 genomic sequence;
- e.) 74651C of the human aminopeptidase P genomic sequence; and
- f.) 74651T of the human aminopeptidase P genomic sequence.
- 25 28) A method for identifying an individual at risk of developing a disorder upon administration of a pharmaceutically acceptable amount of an ACE inhibitor and/or vasopeptidase inhibitor comprising the steps of
- a.) obtaining nucleic acid sample(s) from said individual;
- 30 b.) amplifying one or more sequences from said sample(s) using appropriate PCR primers for amplifying across at least one polymorphic position;
- c.) comparing said at least one polymorphic position with a known data set; and
- 35 d.) determining whether the result correlates with an increased or decreased risk for developing a disorder.

- 5 29) The method according to claim 28 wherein said at least one polymorphic position is selected from the group consisting of:
- a.) 62738 of the human bradykinin receptor B2 genomic sequence;
- b.) 4627 of the human kallikrein 1 genomic sequence; and
- 10 c.) 74651 of the human aminopeptidase P genomic sequence.
- 30) The isolated nucleic acid of claim 29 wherein said at least one polymorphic position is selected from the group consisting of:
- a.) 62738T of the human bradykinin receptor B2 genomic sequence;
- 15 b.) 62738A of the human bradykinin receptor B2 genomic sequence;
- c.) 4627C of the human kallikrein 1 genomic sequence;
- d.) 4627T of the human kallikrein 1 genomic sequence;
- 20 e.) 74651C of the human aminopeptidase P genomic sequence; and
- f.) 74651T of the human aminopeptidase P genomic sequence.
- 31) The method of claim 30 wherein the disorder is angioedema or an angioedema-like disorder.
- 25 32) A library of nucleic acids, each of which comprises one or more polymorphic positions within a gene encoding a human protein selected from the group consisting of aminopeptidase P protein (XPNPEP2), bradykinin receptor B1 protein (BDKRB1), tachykinin receptor 1 protein (TACR1), C1 esterase inhibitor protein (C1NH), kallikrein 1 protein (KLK1), bradykinin receptor B2 protein (BDKRB2), angiotension converting enzyme 2 protein (ACE2), and protease inhibitor 4 protein (PI4), wherein said polymorphic positions
- 30 are selected from a group consisting of the polymorphic positions provided in Table V.
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- 5 33) The library of nucleic acids of claim 32 wherein the sequence at said polymorphic position is selected from the group consisting of the sequences provided in Table V.
- 34) The library according to claim 33 wherein the polymorphic position is a member of the group consisting of:
- 10 a.) 62738 of the human bradykinin receptor B2 genomic sequence;
- b.) 4627 of the human kallikrein 1 genomic sequence; and
- c.) 74651 of the human aminopeptidase P genomic sequence.
- 15 35) The library according to claim 34 wherein the sequence at the polymorphic position is a member of the group consisting of:
- a.) 62738T of the human bradykinin receptor B2 genomic sequence;
- b.) 62738A of the human bradykinin receptor B2 genomic sequence;
- 20 c.) 4627C of the human kallikrein 1 genomic sequence;
- d.) 4627T of the human kallikrein 1 genomic sequence;
- e.) 74651C of the human aminopeptidase P genomic sequence; and
- 25 f.) 74651T of the human aminopeptidase P genomic sequence.
- 36) The library according to claim 35 wherein said library of isolated sequences represents the complimentary sequence of said sequences.
- 30 37) A kit for identifying an individual at risk of developing a disorder upon administration of a pharmaceutically acceptable amount of an ACE inhibitor and/or vasopectidase inhibitor, said kit comprising
- i.) sequencing primers, and
- ii.) sequencing reagents,
- wherein said primers are primers that hybridize to at least one
- 35 polymorphic position in a human gene selected from the group consisting of aminopeptidase P protein (XPNPEP2), bradykinin

- 5 receptor B1 protein (BDKRB1), tachykinin receptor 1 protein (TACR1), C1 esterase inhibitor protein (C1NH), kallikrein 1 protein (KLK1), bradykinin receptor B2 protein (BDKRB2), angiotension converting enzyme 2 protein (ACE2), and protease inhibitor 4 protein (PI4).
- 10 38) The kit according to claim 37 wherein said polymorphic positions are selected from a group consisting of the polymorphic positions provided in Table V.
- 39) The kit according to claim 38 wherein the polymorphic position is a member of the group consisting of:
- 15 a.) 62738 of the human bradykinin receptor B2 genomic sequence;
- b.) 4627 of the human kallikrein 1 genomic sequence; and
- c.) 74651 of the human aminopeptidase P genomic sequence.
- 20 40) The kit according to claim 39 wherein the sequence at the polymorphic position is a member of the group consisting of:
- a.) 62738T of the human bradykinin receptor B2 genomic sequence;
- b.) 62738A of the human bradykinin receptor B2 genomic sequence;
- 25 c.) 4627C of the human kallikrein 1 genomic sequence;
- d.) 4627T of the human kallikrein 1 genomic sequence;
- e.) 74651C of the human aminopeptidase P genomic sequence; and
- 30 f.) 74651T of the human aminopeptidase P genomic sequence.
- 41) The kit according to claim 40 wherein said primer(s) hybridizes immediately adjacent to said polymorphic positions.

- 5 42) The kit according to claim 41 wherein said primer(s) hybridizes to said polymorphic positions such that the central position of the primer aligns with the polymorphic position of said gene.
- 43) The method according to claim 28 further comprising the step of
10 subjecting the product(s) of said amplification to a genetic bit analysis (GBA) reaction.
- 44) A method for identifying an individual at risk of developing a disorder upon administration of a pharmaceutically acceptable amount of an ACE inhibitor and/or vasopeptidase inhibitor comprising the steps of
- a.) obtaining a nucleic acid sample(s) from said individual;
15 b.) determining the nucleotide present at least one polymorphic position,
 c.) comparing said at least one polymorphic position with a known data set; and
 d.) determining whether the result correlates with an increased or decreased risk for developing a disorder.
- 20 45) The method according to claim 44 wherein said at least one polymorphic position is selected from the group consisting of:
- a.) 62738 of the human bradykinin receptor B2 genomic sequence;
25 b.) 4627 of the human kallikrein 1 genomic sequence; and
 c.) 74651 of the human aminopeptidase P genomic sequence.
- 46) The isolated nucleic acid of claim 45 wherein said at least one polymorphic position is selected from the group consisting of:
- 30 a.) 62738T of the human bradykinin receptor B2 genomic sequence;
 b.) 62738A of the human bradykinin receptor B2 genomic sequence;
 c.) 4627C of the human kallikrein 1 genomic sequence;
35 d.) 4627T of the human kallikrein 1 genomic sequence;

- 5 e.) 74651C of the human aminopeptidase P genomic sequence; and
- f.) 74651T of the human aminopeptidase P genomic sequence.
- 10 47) The method of claim 46 wherein the disorder is angioedema or an angioedema-like disorder.
- 48) A method for genotyping an individual comprising the steps of
- a.) obtaining a nucleic acid sample(s) from said individual;
- b.) determining the nucleotide present at least one polymorphic position, and
- 15 c.) comparing said at least one polymorphic position with a known data set.
- 49) The method according to claim 48 wherein said at least one polymorphic position is selected from the group consisting of:
- a.) 62738 of the human bradykinin receptor B2 genomic sequence;
- 20 b.) 4627 of the human kallikrein 1 genomic sequence; and
- c.) 74651 of the human aminopeptidase P genomic sequence.
- 50) The isolated nucleic acid of claim 49 wherein said at least one polymorphic position is selected from the group consisting of:
- 25 a.) 62738T of the human bradykinin receptor B2 genomic sequence;
- b.) 62738A of the human bradykinin receptor B2 genomic sequence;
- 30 c.) 4627C of the human kallikrein 1 genomic sequence;
- d.) 4627T of the human kallikrein 1 genomic sequence;
- e.) 74651C of the human aminopeptidase P genomic sequence; and
- 35 f.) 74651T of the human aminopeptidase P genomic sequence.